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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/727,480	12/04/2000	Sara Alajem	00/21400	4363

7590 02/27/2003

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EXAMINER
FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
1634	15

DATE MAILED: 02/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/727,480	ALAJEM ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *87-92* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *87-92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 23, 2003 has been entered.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 87-92 are rejected under 35 U.S.C. 102(b) as being anticipated by Hogan et al (U.S. Patent 5,451,503).

Hogan teaches a method for detecting the presence or the absence of a target nucleic acid sequence in a sample (column 6 and column 35, claim 1) comprising the steps:

a) contacting the sample with an oligonucleotide system under hybridization conditions so as to form a reaction mixture (see figure 15 E) where said oligonucleotide system includes two oligonucleotides, one "anchor oligonucleotide" which has two regions, one which hybridizes to the target and one which hybridizes to an "amplifier oligonucleotide" (see figure 15 E) and where the "amplifier oligonucleotide" also has two

regions, one which hybridizes to the target and one which hybridizes to the "anchor oligonucleotide" (see figure 15 E), which includes a sequence which, upon formation of a duplex, will be recognized by the nuclease cleavage reagent RNAse H (figure 15 E) and where the RNAse H cleavage reagent will cleave only the "amplifier oligonucleotide" but not the "anchor oligonucleotide" (see figure 15 E) and where cleavage of the "amplifier oligonucleotide" leads to the dissociation of the "anchor oligonucleotide" (see column 21, lines 45-57 and column 22, lines 10-16), thus enabling recycling of the anchor oligonucleotide target sequence hybrid with respect to the amplifier oligonucleotide (see column 22, lines 10-16)

b) adding a cleaving agent, where the nuclease may include RNAse H, which cleaves only the RNA strand and not the DNA strand, thus cleaving only a single strand (column 4, lines 21-54) and permitting recycling (see column 22, lines 10-16),

c) monitoring the presence or absence of cleavage products (column 36, claim 6, column 37, claim 7 or column 6, line 31 to column 7, line 24).

Hogan expressly teaches the instance where cleavage of the arm regions reduces the stability of the complex, thereby resulting in dissociation of the probe regions from the target (column 21, lines 33-42).

Hogan expressly teaches the use of modified nucleotides in the probes such as phosphorothioates which prevent cleavage by the cleaving agent (column 6, lines 11-26).

Hogan further expressly teaches that this dissociation can enable a second assembly to hybridize with the target sequence (column 21, lines 39-42).

Hogan teaches the use of probes where the Tm of the regions differ by 10 C (see column 2, lines 60-64).

Response to Arguments

4. Applicant's arguments filed January 23, 2003 have been fully considered but they are not persuasive.

Applicant argues that a distinction between their invention and the prior art of Hogan is that Hogan does not teach oligonucleotide-target recycling. This argument is not persuasive for several reaons. First, Hogan expressly teaches recycling as discussed both by applicant and by the rejection. The issue of what constitutes target is broad in this context and the sequence recycled by Hogan is a target. This is made particularly clear where Hogan states "This will then allow uncleaved probe strands to hybridize with the target and start the process over again, thus increasing assay sensitivity by cycling multiple probes through a single target site (column 21, lines 39-42)". With regard to the particular embodiment closest in style to Applicant's, Hogan notes "This system also has the potential for cycling as described above (see column 22, lines 15-17)". Thus, it is clear that Hogan contemplates, teaches and uses cycling technology.

Second, Applicant discusses how the Anchor oligonucleoitde and amplifier are specifically designed to have particular Tms higher than the reaction temperature to hybridize solely in the presence of hybridized anchor oligonucleotide. These limitations are expressly shown by Hogan and do not distinguish from the Hogan reference. As

noted in the rejection, Hogan teaches that it is preferred for the probes to have Tms of 10 C lower (see column 2).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1637

February 24, 2003